CLAIMS

1. The process comprising preparing dibenzyl 7-azabicyclo[2.2.1]heptane-2,7-dicarboxylate (**4**) from phenyl 2-bromo-3-oxo-8-azabicyclo[3.2.1]octane-8-carboxylate (**3**), comprising dissolving **3** in water or an organic solvent, optionally adding **3** as a ca. 50% w/v solution in a suitable solvent, optionally toluene,

further comprising adding a base,

further optionally comprising conducting the reaction at a temperature from about –10°C to about 50°C, and

further comprising isolating **4**, optionally having stereochemical purity of *exo* versus *endo* ratio being about 100:1.

2. The process of claim 1, wherein the organic solvent includes toluene, acetonitrile, dimethoxyethane, diethyl ether, methanol, ethanol, isopropanol, or benzyl alcohol.

3. The process of claim 2, wherein the organic solvent is benzyl alcohol.

4. The process of claim 2, wherein from about 1 eq to about 3 eq of base are used.

5. The process of claim 4, wherein the base includes sodium or potassium hydroxide, or the sodium or potassium salts of the alcoholic solvent.

6. The process of claim 5, wherein 2.2 eq of this base are used.

7. The process of claim 5, wherein the base is sodium benzyloxide.

8. The process of claim 5, wherein the reaction is conducted at a concentration from about 3 mL to about 10 mL of solvent per gram of **3**.

9. The process of claim 8, wherein about 4 mL of solvent are used per gram of **3**.

10. The process of claim 8, wherein the reaction is conducted at about 5°C.

11. The process of claim 8, wherein the reaction is allowed to stir for about 1 hour or until less than 1% of bromoketone **3** or the corresponding benzyl carbamate remains.

12. The process of claim 11, wherein **4** is isolated further comprising diluting the reaction mixture with 1:1 heptane/toluene;

further comprising neutralizing with conc. HCl;

further comprising extracting the organic phase with aqueous NaOH;

further comprising washing with brine, drying over a drying agent, filtering, and concentrating using standard procedures; and

further comprising removal of excess benzyl alcohol.

13. The process of claim 12, wherein the drying agent is Na_2SO_4.

14. The process of claim 12, wherein the concentrating occurs under reduced pressure at low temperature.

15. The process of claim 14, wherein the temperature is about 40°C.

16. The process of claim 12, wherein the benzyl alcohol is removed by distillation.

17. The process of claim 16, wherein the distillation occurs at about 5 mmHg with a bath temperature of up to 90°C.

18. The process of claim 12, wherein **4** is obtained with as a ratio of about 100:1 that is *exo/endo*.

19. The process of claim 1, further comprising preparing **3** from phenyl 3-oxo-8-azabicyclo[3.2.1]octane-8-carboxylate (**2**), comprising dissolving **2** in an inert organic solvent,

further comprising heating the reaction,

further comprising adding anhydrous $CuBr_2$,

further comprising isolating **3**.

20. The process of claim 19, wherein the inert organic solvent includes toluene, acetonitrile, chloroform, an ethyl acetate/chloroform mixture, or ethyl acetate.

21. The process of claim 20, wherein the solvent is ethyl acetate.

22. The process of claim 19, wherein the amount of solvent used is from about 5 mL to about 20 mL of solvent per gram of **2**.

23. The process of claim 22, wherein the amount of solvent used is about 10 mL per gram of **2**.

24. The process of claim 19, wherein the reaction is heated from about 50°C to about 110°C.

25. The process of claim 24, wherein the reaction is conducted by refluxing in EtOAc.

26. The process of claim 19, wherein from about 1.9 to about 2.1 eq of $CuBr_2$ are used.

27. The process of claim 26, wherein 2.0 eq are used.

28. The process of claim 19, wherein the reaction is allowed to stir until **2** is less than 1%.

29. The process of claim 19, wherein **3** is isolated using 1 or more suitable solvents, optionally a solution of toluene being from about 25 to about 75% w/v;

further comprising filtering off the CuBr;

further comprising washing the product solution with water and aqueous $NaHCO_3$, optionally 5%, removing the EtOAc; and

further comprising adding suitable solvent to give the desired concentration.

30. The process of claim 19, further comprising preparing **2** from tropinone, comprising dissolving tropinone in an inert organic reaction solvent,

further comprising adding a weak insoluble inorganic base,

further comprising conducting the reaction at a temperature of at least about 0°C,

further comprising adding phenyl chloroformate, optionally heating to reflux after addition is complete,

further comprising isolating **2**.

31. The process of claim 30, wherein the inert organic solvent includes toluene, acetonitrile, dichloromethane, or ethyl acetate.

32. The process of claim 30, wherein the weak insoluble inorganic base includes sodium or potassium bicarbonate or sodium or potassium carbonate.

33. The process of claim 30, wherein the reaction is heating from about 0°C to about 110°C.

34. The process of claim 30, wherein the chloroformate is added at a rate to keep the reaction temperature less than about 30°C.

35. The process of claim 30, wherein **2** is isolated comprising slowly adding an antisolvent;

further comprising cooling the reaction from about –10°C to about 20°C;

further comprising removing **2** by filtration, washing with a dilute acid solution;

further comprising washing with water; and

optionally further comprising washing with a dilute base solution.

36. The process of claim 35, wherein the antisolvent is hexane or heptane.

37. The process of claim 35, wherein an amount of antisolvent is used to give a concentration of about 1 mL to about 5 mL of antisolvent per mL of reaction solvent.

38. The process of claim 37, wherein about 2 mL of antisolvent per mL of solvent are used.

39. The process of claim 35, wherein the dilute acid solution is from about 0.5% to about 5%.

40. The process of claim 39, wherein the dilute acid solution includes sulfuric, phosphoric, or hydrochloric acid.

41. The process of claim 35, wherein the optional dilute base solution is from about 0.5% to about 5%.

42. The process of claim 35, wherein **2** is obtained with about 99% purity.

43. The process of claim 30, further comprising the preparation of 7-(*tert*-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid (**6**) from **4**, comprising dissolving **4** in a low molecular weight alcohol, optionally ethanol or isopropanol;

further comprising using Pd/C, optionally 5-10% Pd/C and optionally from about 0.5 to about 5 g of Pd/C per gram of **4**;

further comprising applying hydrogen, optionally from about 30 psi to about 60 psi and further optionally at a temperature of at least room temperature;

further comprising isolating 7-azabicyclo[2.2.1]heptane-2-carboxylic acid (**5b**);

further comprising dissolving **5b** in THF and acqueous KOH, optionally 10% aqueous, to give a homogeneous solution, optionally adding aqueous KOH more than once;

further comprising adding $(BOC)_2O$, optionally adding $(BOC)_2O$ more than once; and

further comprising isolating **6**.

44. The process of claim 43, further comprising preparing *exo-tert*-butyl 2(*R*(+)-{[(benzyloxy)carbonyl]amino}-7-azabicyclo[2.2.1]heptane-7-carboxylate (**8**) from **6**, by resolving (2*R*)-7-(*tert*-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid (**15**) from **6**;

further comprising dissolving **15** and a non-nucleophilic organic soluble base, optionally Et_3N and optionally from about 1 eq to about 1.5 eq, in toluene;

further comprising heating the solution, optionally from about 30°C to about 80°C;

further comprising adding DPPA, optionally from about 0.95 eq to about 1.2 eq, and further optionally at a rate to control the reaction temperature and nitrogen off-gassing rate;

further comprising heating the reaction, optionally from about 30°C to 110°C, once the temperature and nitrogen off gassing begins to fall;

further comprising adding benzyl alcohol, optionally from about 0.95 eq to about 1.5 eq;

further comprising stirring the reaction, optionally at a temperature from about 30°C to 110°C and optionally for about 1 hour or until residual **15** is less than 1% relative to **8**;

further comprising a mildly basic aqueous work-up, optionally purifying using silica gel chromatography eluting with EtOAc, optionally 40-50% EtOAc in hexane; and

further comprising isolating **8**.

45. The process of claim 44, further comprising preparing *exo*-(t-butyl 2*R*(+))-2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate (**1**) from **8** by hydrogenolysis.

46. The process of claim 43, further comprising preparing *exo-tert*-butyl 2(*R*(+)-{[(benzyloxy)carbonyl]amino}-7-azabicyclo[2.2.1]heptane-7-carboxylate (**8**) from *tert*-butyl 2-{[(benzyloxy)carbonyl]amino}-7-azabicyclo[2.2.1]heptane-7-carboxylate (**7**) after preparing **7** from **6**;

further comprising dissolving **6** and a non-nucleophilic organic soluble base, optionally from about 1 to about 1.5 equivalents relative to substrate **6** and optionally using triethylamine or diisopropyl ethylamine as the base, in a high-boiling, inert organic solvent, optionally toluene or xylene and optionally to give a resulting concentration of solvent to substrate of about 3 mL to about 10 mL of solvent per gram of substrate;

further comprising heating the solution, optionally from about 30°C to about 80°C;

further comprising adding DPPA, optionally from about 0.95 to about 1.2 equivalents and optionally at a rate to control the reaction temperature and nitrogen off-gassing rate;

further comprising heating the reaction, optionally from about 30°C to about 110°C once the temperature and nitrogen off gassing begins to fall;

further comprising adding benzyl alcohol, optionally from about 0.95 to about 1.5 eq, and heating the reaction, optionally at from about 30°C to 110°C and optionally until residual **6** is less than 1% relative to **7** or about 1 hour after addition of benzyl alcohol;

further comprising a mildly basic aqueous work-up, optionally $NaHCO_3$;

further comprising isolating **7**;

further comprising crystallizing **7** from hexane/ethyl acetate; and

further comprising resolving **8** from **7**.

47. The process of claim 46, further comprising preparing *exo*-(t-butyl 2*R*(+))-2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate (**1**) from **8** by hydrogenolysis.

48. The process of claim 1, further comprising the preparation of 7-(*tert*-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid (**6**) from **4**, comprising dissolving **4** in a low molecular weight alcohol, optionally ethanol or isopropanol;

further comprising using Pd/C, optionally 5-10% Pd/C and optionally from about 0.5 to about 5 g of Pd/C per gram of **4**;

further comprising applying hydrogen, optionally from about 30 psi to about 60 psi and further optionally at a temperature of at least room temperature;

further comprising isolating 7-azabicyclo[2.2.1]heptane-2-carboxylic acid (**5b**);

further comprising dissolving **5b** in THF and acqueous KOH, optionally 10% aqueous, to give a homogeneous solution, optionally adding aqueous KOH more than once;

further comprising adding $(BOC)_2O$, optionally adding $(BOC)_2O$ more than once; and

further comprising isolating **6**.

49. The process of claim 48, further comprising preparing *exo-tert*-butyl 2(*R*(+)-{[(benzyloxy)carbonyl]amino}-7-azabicyclo[2.2.1]heptane-7-carboxylate (**8**) from **6**,

by resolving (2*R*)-7-(*tert*-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid (**15**) from **6**;

further comprising dissolving **15** and a non-nucleophilic organic soluble base, optionally Et_3N and optionally from about 1 eq to about 1.5 eq, in toluene;

further comprising heating the solution, optionally from about 30°C to about 80°C;

further comprising adding DPPA, optionally from about 0.95 eq to about 1.2 eq, and further optionally at a rate to control the reaction temperature and nitrogen off-gassing rate;

further comprising heating the reaction, optionally from about 30°C to 110°C, once the temperature and nitrogen off gassing begins to fall;

further comprising adding benzyl alcohol, optionally from about 0.95 eq to about 1.5 eq;

further comprising stirring the reaction, optionally at a temperature from about 30°C to 110°C, for about 1 hour or until residual **15** is less than 1% relative to **8**;

further comprising a mildly basic aqueous work-up, optionally purifying using silica gel chromatography eluting with EtOAc, optionally 40-50% EtOAc in hexane; and

further comprising isolating **8**.

50. The process of claim 49, further comprising preparing *exo*-(t-butyl 2*R*(+))-2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate (**1**) from **8** by hydrogenolysis.

51. The process of claim 48, further comprising preparing *exo-tert*-butyl 2(*R*(+)-{[(benzyloxy)carbonyl]amino}-7-azabicyclo[2.2.1]heptane-7-carboxylate (**8**) from *tert*-butyl 2-{[(benzyloxy)carbonyl]amino}-7-azabicyclo[2.2.1]heptane-7-carboxylate (**7**) after preparing **7** from **6**;

further comprising dissolving **6** and a non-nucleophilic organic soluble base, optionally from about 1 to about 1.5 equivalents relative to substrate **6** and optionally using triethylamine or diisopropyl ethylamine as the base, in a high-boiling, inert organic solvent, optionally toluene or xylene and optionally to give a resulting concentration of solvent to substrate of about 3 mL to about 10 mL of solvent per gram of substrate;

further comprising heating the solution, optionally from about 30°C to about 80°C;

further comprising adding DPPA, optionally from about 0.95 to about 1.2 equivalents and optionally at a rate to control the reaction temperature and nitrogen off-gassing rate;

further comprising heating the reaction from about 30°C to about 110°C once the temperature and nitrogen off gassing begins to fall;

further comprising adding benzyl alcohol, optionally from about 0.95 to about 1.5 eq, and heating the reaction at from about 30°C to 110°C, until residual **6** is less than 1% relative to **7** or about 1 hour after addition of benzyl alcohol;

further comprising a mildly basic aqueous work-up, optionally $NaHCO_3$;

further comprising isolating **7**;

further comprising crystallizing **7** from hexane/ethyl acetate; and

further comprising resolving **8** from **7**.

52. The process of claim 51, further comprising preparing *exo*-(t-butyl 2*R*(+))-2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate (**1**) from **8** by hydrogenolysis.

53. The process of claim 1 further comprising preparing 7-(*tert*-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid (**6**) from *tert*-butyl 3-oxo-8-azabicyclo[3.2.1]octane-8-carboxylate (**12**), comprising treating **12** with an amine base, wherein the base is optionally diazabicycloundecene or DBU, and TMS-Cl to give a silyl enol ether intermediate;

further comprising treating the enol intermediate in EtOAc with TCCA to give a chlorinated intermediate;

further optionally comprising isolating the chlorinated intermediate and optionally removing EtOAc and toluene; and

further comprising treating the chlorinated intermediate with a base including KOH in an alcoholic solvent, optionally isopropanol, or NaOH in an alcoholic solvent, optionally ethanol.

54. The process of claim 53, further comprising preparing **12** from tropinone, comprising addition of triphosgene to tropinone in an inert solvent, optionally toluene;

further comprising addition of water;

further comprising adding an aqueous base, optionally NaOH, to raise the reaction pH, optionally above 10;

further optionally comprising the addition of more toluene; and

further comprising addition of $(BOC)_2O$, optionally comprising the addition of DMAP to catalyze the destruction of residual $(BOC)_2O$ and isolation of **12**.

55. The process of claim 54, further comprising addition of neat DBU, optionally 1.4 eq, and followed by the addition of neat TMS-Cl, optionally 1.3 eq, to **12** in toluene in that order;

further comprising isolating the enol intermediate;

further comprising the addition of solid TCCA to the enol intermediate in EtOAc optionally cooled to about 0-5°C, and further optionally stirring at 0°C until the enol intermediate is consumed; and

further comprising isolating the chlorinated intermediate and removing EtOAc and toluene.

56. The process of claim 55, further comprising preparing *exo-tert*-butyl 2(*R*(+)-{[(benzyloxy)carbonyl]amino}-7-azabicyclo[2.2.1]heptane-7-carboxylate (**8**) from **6**, by resolving (2*R*)-7-(*tert*-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid (**15**) from **6**;

further comprising dissolving **15** and a non-nucleophilic organic soluble base, optionally Et_3N and optionally from about 1 eq to about 1.5 eq, in toluene;

further comprising heating the solution, optionally from about 30°C to about 80°C;

further comprising adding DPPA, optionally from about 0.95 eq to about 1.2 eq, and further optionally at a rate to control the reaction temperature and nitrogen off-gassing rate;

further comprising heating the reaction, optionally from about 30°C to 110°C, once the temperature and nitrogen off gassing begins to fall;

further comprising adding benzyl alcohol, optionally from about 0.95 eq to about 1.5 eq;

further comprising stirring the reaction, optionally at a temperature from about 30°C to 110°C and optionally for about 1 hour or until residual **15** is less than 1% relative to **8**;

further comprising a mildly basic aqueous work-up, optionally purifying using silica gel chromatography eluting with EtOAc, optionally 40-50% EtOAc in hexane; and

further comprising isolating **8**.

57. The process of claim 56, further comprising preparing *exo*-(t-butyl 2*R*(+))-2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate (**1**) from **8** by hydrogenolysis.

58. The process of claim 55, further comprising preparing *exo-tert*-butyl 2(*R*(+)-{[(benzyloxy)carbonyl]amino}-7-azabicyclo[2.2.1]heptane-7-carboxylate (**8**) from *tert*-butyl 2-{[(benzyloxy)carbonyl]amino}-7-azabicyclo[2.2.1]heptane-7-carboxylate (**7**) after preparing **7** from **6**;

further comprising dissolving **6** and a non-nucleophilic organic soluble base, optionally from about 1 to about 1.5 equivalents relative to substrate **6** and optionally using triethylamine or diisopropyl ethylamine as the base, in a high-boiling, inert organic solvent, optionally toluene or xylene and optionally to give a resulting concentration of solvent to substrate of about 3 mL to about 10 mL of solvent per gram of substrate;

further comprising heating the solution, optionally from about 30°C to about 80°C;

further comprising adding DPPA, optionally from about 0.95 to about 1.2 equivalents and optionally at a rate to control the reaction temperature and nitrogen off-gassing rate;

further comprising heating the reaction from about 30°C to about 110°C once the temperature and nitrogen off gassing begins to fall;

further comprising adding benzyl alcohol, optionally from about 0.95 to about 1.5 eq, and heating the reaction at from about 30°C to 110°C, until residual **6** is less than 1% relative to **7** or about 1 hour after addition of benzyl alcohol;

further comprising a mildly basic aqueous work-up, optionally $NaHCO_3$;

further comprising isolating **7**;

further comprising crystallizing **7** from hexane/ethyl acetate; and

further comprising resolving **8** from **7**.

59. The process of claim 58, further comprising preparing *exo*-(t-butyl 2*R*(+))-2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate (**1**) from **8** by hydrogenolysis.

60. A compound that is

exo-(*tert*-butyl 2*R*(+))-2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate (**1**);

exo-tert-butyl 2(R(+)-{[(benzyloxy)carbonyl]amino}-7-azabicyclo[2.2.1]heptane-7-carboxylate (**8**);

exo-tert-butyl 2-[(benzyloxy)carbonyl]amino-7-azabicyclo[2.2.1]heptane-7-carboxylate (**7**);

(2*R*)-7-(*tert*-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid (**15**); or

7-(*tert*-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid (**6**),

provided that when the compound is an acid, the compound can be an alkali metal or amine salt thereof; further provided that when the compound is an amine, the compound can be an acid salt thereof; and further provided that the compound can have varying degrees of chemical purity and chiral purity.

61. The compound of claim 60 that is *exo*-(t-butyl 2*R*(+))-2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate (**1**), provided that the compound can be the acid salt thereof; and further provided that the compound can have varying degrees of chemical purity and chiral purity.

62. The compound of claim 61, wherein the compound has at least 95% chemical purity and at least 95% chiral purity.

63. The compound of claim 61, wherein the compound has at least 97% chemical purity and at least 99.5% chiral purity.

64. The compound of claim 60 that is 7-(*tert*-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid (**6**), provided that the compound can be the alkali metal or amine salt thereof, and further provided that the compound can have varying degrees of chemical purity and chiral purity.

65. The compound of claim 64, wherein the compound has at least 95% chemical purity and at least 95% chiral purity.

66. The compound of claim 64, wherein the compound has at least 97% chemical purity and at least 99.5% chiral purity.